REMARKS

A. Status of the Claims

Claims 1-5 were pending at the issuance of the instant Office Action mailed on September 4, 2008. Claims 1, 3, and 4 have been amended. Claim 2 has been canceled, the subject matter thereof having been incorporated in Claim 1. No new matter has been added as a result of the amendments.

B. Claim Rejections – 35 USC §112

Claims 1-5 are rejected under 35 USC §112, second paragraph as allegedly indefinite as to the term "MS-275." Applicant submits that the term "MS-275" is not indefinite, because those of skill in the art at the time the present application was filed recognized that MS-275 was an HDAC inhibitor. As stated in MPEP §2173.02, a claim term that is not used or defined in the specification is not indefinite if the meaning of the claim term is discernible. *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004). One of skill in the art can readily discern the structure of MS-275 through routine literature searches. Thus, the claims are not indefinite. Consequently, Applicant respectfully requests that this ground of rejection be withdrawn.

Claims 1-5 are also rejected under 35 USC §112, first paragraph as allegedly failing to comply with the written description requirement. The Action asserts that the claims are drawn to unspecified diseases, and that the use of the term "depsipeptides" is not supported by the specification as filed. Claim 1 has been amended without prejudice or disclaimer, solely to expedite prosecution, to incorporate the specific disorders and diseases that were mentioned in original Claim 2, and no longer recites "depsipeptides." Consequently, these grounds of rejection have been rendered moot.

C. Claim Rejections – 35 USC §103

Claims 1-3 and 5 stand rejected under 35 USC §103 as unpatentable over Bressi *et al.* Specifically, the Action contends that it would have been obvious to use the claimed compound to treat degenerative conditions of the eye, because the teaching of Bressi *et al.* "teaches the use of the claimed compound, SAHA as a histone deacetylase inhibitor, and also the use of histone deacetylase inhibitors for the treatment of macular degeneration, diabetic retinopathy and glaucoma" (Office Action, page 4). The Action also contends that macular degeneration, diabetic retinopathy and glaucoma are degenerative disorders. Applicant respectfully traverses.

As stated in MPEP 2143(B), "the rationale to support a conclusion that the claim would have been obvious is that the substitution of one known element for another yields predictable results to one of ordinary skill in the art. If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art." As stated in MPEP 2143.02(II), "obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness" (citing *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)).

Applicant respectfully submits that one of skill in the art would not have considered substitution of any of the Bressi compounds with one of the compounds of the instant claims to yield predictable results or to have a reasonable expectation of success to treat the diseases and disorders recited in the instant claims, because the teaching of Bressi *et al.* relates specifically to abnormal angiogenesis and a specific genus of compounds.

Bressi *et al.* teach several HDAC inhibitor compounds related by the general formula shown in the Abstract of US Patent No. 7,154,002 ("the '002 patent"). As discussed in Col. 53, Example 3, of the '002 patent, Bressi *et al.* demonstrated that the compounds had varying activities against the HDAC8 isoform, where only some had better than 5 μM activity (see Figures 5A and 5B). The Bressi compounds were not tested for activity against other HDACs. Even though Bressi *et al.* mention that the compounds may be used as inhibitors of

Class I HDACs (Col. 11, lines 52-54), there is absolutely no evidence that such compounds can inhibit any of the isoforms in Class I other than HDAC8 (*i.e.* HDAC1, 2, 3, or 11). Further, Bressi *et al.* mention (but do not claim) several examples of HDAC inhibitors, such as SAHA; however, only the claimed compounds are taught to be useful for treating the various diseases listed in the Bressi patent. Thus, Bressi *et al.* teach that a *specific* genus of HDAC inhibitors active against HDAC8 are useful for treating macular degeneration and diabetic retinopathy, but do not teach that *all* HDAC inhibitors are useful for such a purpose. Therefore, one of skill in the art could not have known whether it was activity against HDAC8 specifically or against any HDAC isoform (or any combination of HDAC isoforms) that would be useful for treating the many diseases listed in the Bressi patent. Consequently, based on the teaching by Bressi *et al.*, use of HDAC inhibitors other than those specifically falling in the genus of claimed compounds in Bressi would not have been predictable.

As pointed out by Bressi *et al.*, numerous human HDACs were known at the time the Bressi application was filed, and were categorized into three distinct classes (see col. 11, lines 55-67). It is well established that not all of the HDAC inhibitors share exactly the same activity (*e.g.* some are selective for particular HDAC isoforms, while others non-selectively act on multiple isoforms), and that different HDAC isoforms can regulate different sets of genes. Consequently, the universe of HDAC inhibitors is diverse and very large, and substitution of one HDAC inhibitor for another would not necessarily lead to a predictable result.

The instant claims are directed toward a small subset of that very large universe. The Federal Circuit in *Eisai Co. v. Dr. Reddy's Labs* has indicated that

> the Supreme Court's analysis in *KSR* presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a 'finite number of identified, predictable solutions." (*Eisai Co. v. Dr. Reddy's Labs, Ltd.*, 487 USPQ2d 1452 (Fed. Cir. 2008) citing *KSR Int'l Co. v. Teleflex*, 127 S. Ct. at 1742.

Bressi *et al.* certainly did not provide such reasons for narrowing the HDAC inhibitor universe to the compounds of the instant claims. Applicant submits that there is no teaching or suggestion in the '002 patent, or in the art at the time the instant application was filed, that

would have motivated one of skill in the art to select the particular compounds of the instant claims to treat a degenerative disorder or disease recited in the claims. The Action does not set forth any specific evidence or reasoning that would demonstrate otherwise.

Bressi *et al.* disclosed many examples of HDAC inhibitors, but only indicated that the specifically claimed compounds may be useful for treating diseases associated with abnormal angiogenesis. As stated in MPEP 2142,

> The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also *KSR*, 550 U.S. at ___ , 82 USPQ2d at 1396 (quoting Federal Circuit statement with approval).

The Action has not provided a rational reasoning as to why one of skill in the art would have been motivated to select the particular compounds of the instant claims based on the narrow teaching of Bressi *et al.* that specifically relates to a particular genus of HDAC inhibitors and not to HDAC inhibitors in general. The Action's reasoning amounts to a mere conclusory statement rather than an explicit analysis. Consequently, the Action has not supported the obviousness rejection it proposes.

Further, there is no teaching or suggestion in Bressi *et al.* that *any* HDAC inhibitor would be useful for treating the various diseases taught in the '002 patent. Rather, Bressi *et al.* emphasize that the particular compounds of the '002 patent claims (which specifically act on HDAC8) may be useful for such treatments, not the other HDAC inhibitors that are disclosed but not claimed in the Bressi *et al.* patent. Thus, there is no reasonable expectation of success for substituting an HDAC inhibitor of the instant claims for one of the HDAC inhibitors of the Bressi claims, absent specific evidence to the contrary.

In light of the foregoing arguments, Applicant respectfully requests that this ground of rejection be withdrawn.

D. Conclusion

This is submitted to be a complete response to the outstanding Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

The Examiner is invited to contact the undersigned attorney at (817) 615-5330 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

/Jason J. Derry, #50,692/

Jason J. Derry
Reg. No. 50,692
Attorney for Applicants

ALCON RESEARCH, LTD.
6201 S. Freeway, TB4-8
Fort Worth, TX 76134-2099
(817) 615-5330

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